UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,113	03/15/2002	Juerg Lareida	000364.00124	8075

7590 03/23/2004

EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

James J Napoli
Marshall Gerstein & Borun
6300 Sears Tower
233 South Wacker Drive
Chicago, IL 60606-6357

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,113	LAREIDA, JUERG	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3 and 5-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3 and 5-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on November 12, 2003 have been received and entered into the application.

The indicated allowability of claims 5-8 is withdrawn in view of the newly discovered reference(s) herein. Rejections based on the newly cited reference(s) follow.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 2,3 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of **specific** "neuropathy", does not reasonably provide enablement for the treatment of "neuropathies". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the

specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method for treating neuropathies by application of a compound of formula I set forth in claim 5. The nature of the invention is extremely complex in that it encompasses the actual treatment of neuropathies such that the subject treated with above compounds does not contract any neuropathy.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass treatment of a complex cell neuropathy disorder in humans, which has potentially many different causes (i.e. many different diseases or combination of diseases). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually treat all neuropathies is minimal. All of the guidance provided by the specification is directed towards specific neuropathy rather than all neuropathies.

Working Examples: All of the working examples provided by the specification are directed toward the specific neuropathy rather than all neuropathies.

State of the Art: While the state of the art is relatively high with regard to treatment of specific neuropathy (i.e. diabetic neuropathy), the state of the art with regard to treatment of all neuropathies is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to treat all neuropathies.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual treatment of all neuropathies in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of treatment of all neuropathies.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for the treatment of all neuropathies. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard all neuropathies with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If

again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding treatment of all neuropathies with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat all all neuropathies in a subject by administration of one of the claimed compounds.

Therefore, a method of treating neuropathies in a subject applying a compound of formula I set forth in claim 5 is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000.

Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 2, 3 and 5-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Graham (U.S.Patent No. 6,075,028) of record.

Graham teaches a method for treating disorders by administration of an effective amount of sildenafil within Applicant's range. (abstract, claims 1-5).

Applicant's recitation in claims 5, 9 and 10 of an intended use of treating neuropathies would be inherent upon administration of sildenafil in same effective amount to a same patient population.

It is suggested to draw claims to a patient "in need thereof" in order to overcome this rejection.

Claims 2, 3, 5 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Du Bois (U.S.Patent No. 6,399,601B1).

Du Bois teaches a pharmaceutical composition comprising sildenafil for the treatment of diabetic complications such as neuropathy, nephropathy, retinopathy. (abstract, column 23, line 63 through column 24, line 39, particularly, column 24, line 38).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Du Bois (U.S.Patent No. 6,399,601B1) in view of Gentile et al. (1984).

Du Bois teaches a pharmaceutical composition comprising sildenafil for the treatment of diabetic complications such as neuropathy, nephropathy, retinopathy. (abstract, column 23, line 63 through column 24, line 39, particularly, column 24, line 38). Du Bois teaches treatment of diabetic complication, such as neuropathy, nephropathy, retinopathy are included in the treatment of diabetes. (column 23, line 67 though column 24, line 2). Dubois teaches that sildenafil is a representative agent that can be used to treat diabetes. (column 24, lines 18-39).

Du Bois does not teach the specified amounts set forth in claims 6-8 and gastroparesis set forth in claim 10.

Gentile et al. teach diabetic neuropathy of the alimentary canal takes several basic forms including gastorparesis. (abstract).

It would have been obvious to one of ordinary skill in the art to optimized the amount of sildenafil for the treatment of neuropathies since Du Bois teaches that sildenafil comprising composition is useful for the treatment of diabetic complications such as neuropathy, nephropathy. Further, that Du Bois teaches that treatment of neuropathy in diabetic patients encompasses the gastroparesis because diabetic neuropathy takes several basic forms including gastroparesis as taught by Gentile et al. One would have been motivated to employ any basic forms of diabetic neuropathy including gastroparesis by administration of sildenafil in order to achieve effective treatment of diabetic neuropathy in general as taught by Du Bois et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
March 21, 2004